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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/562,478

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Gordana Kosutic

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EXAMINER

LIU, SAMUEL W

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

10/06/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,478	KOSUTIC ET AL.	
	Examiner	Art Unit	
	SAMUEL W. LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) none is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of claims

Claims 1-3 are pending

The terminal disclaimer filed 7/6/09 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US Pat. No.

7084121 has been reviewed and not been approved.

Comment [A1]:

Deleted: .

The amendment filed 7/6/09 which amends claims 1-3 has been entered. Claims 4-13 were cancelled by the amendment filed 12/2/05. Claims 1-3 are under examination.

Priority

Applicant's claim for the benefit of a prior-filed and co-pending application No. 10806523 filed 3/23/04, which is a CON of 09873777 filed 6/04/01 (now US Pat. No. 6713452), under 35 U.S.C. 120 is acknowledged.

However, 10806523 does not disclose instant method of treating peripheral pain using a mixture of conjugate comprising the first and second oligomers covalently linked to Lys¹¹ and Lys¹⁸ of salmon calcitonin. Thus, claims 1-3 are not granted priority to 6/04/01 the filing date of 09/342364 which is parent application of 10806523. Thus, instant invention is entitled to the filed date 6/24/03 of 60482130, which has full support for claims 1-3.

Comment [A2]:

Deleted:

Withdrawn of objections and rejections

(1) The 102/103 rejection of claim 1 is withdrawn in light of the amendment of claim 1.

(2) The 103 rejection of claim 1 by Russo A. and Komarova et al. is withdrawn in light of the amendment of claim 2.

(3) The 103 rejections of (i) claim 2 by Russo A., Komarova et al. and Ekwuribe et al., and (ii) claim 3 by Komarova et al., Ekwuribe N. and Crotts et al. are withdrawn in light of disqualification of the Ekwuribe et al. reference under section 103(c).

Maintained-Objection to specification

The objection set forth in the Office action is maintained because the response filed 7/6/09 does not address said objection.

Maintained- Objection to claims

Claim 1 is objected to because “amine function of Lys¹¹” and “amine function of Lys¹⁸” should be changed to “amine group of Lys¹¹” and “amine group of Lys¹⁸”, respectively.

At pages 4 and 5, the response filed 7/6/09 argues that as the phrases “amine function of Lys¹¹” and “amine function of Lys¹⁸” have been used in the US Pat. No. 7084121, in order to maintain continuity in prosecution, the objection should be withdrawn. The applicants' argument is fully considered but unpersuasive because the specification teaches “coupled to the amino functionalities of Lys¹¹” and “Lys¹⁸” (see [0158], PGPU of this application) but not the "function" thereof, and because the relative art field does not teach that the “function” of amine group can substitute for functional amine group (of functionality) of an amino acid residue.

Maintained-Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1 and 3 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 recite “Lys¹¹” and “Lys¹⁸” without reciting the corresponding SEQ ID NO. The claimed “salmon calcitonin” is broadly but reasonably interpreted as including salmon calcitonin precursor polypeptide or matured polypeptide thereof (see NCBI (2009, updated) calcitonin 1 precursor – salmon, www.ncbi.nlm.nih.gov/protein/2144645?ordinalpos=1&itool=EntrezSystem2.PEntrez.Sequence.Sequence_ResultsPanel.Sequence_RVDocSum, pages 1-2). Provided that the “calcitonin” refers to the precursor calcitonin polypeptide, numbering of “Lys¹¹” and “Lys¹⁸” will not be consistent with the calcitonin precursor polypeptide, Therefore, setting forth said SEQ ID NO is necessary. Otherwise, claims 1 and 3 are indefinite.

The applicants' response to the 112/2 rejection

At page 6, paragraph 5, the response filed 7/6/09 asserts that the claim amendment should obviate the 112/2/ rejection. This is unpersuasive because no said amendment has been made. Thus, the 112/2 is maintained.

Maintained-Claim Rejections - 35 USC §102(e)

The text of Title 35, U.S. C 102(e) not included herein can be found in the prior Office action mailed 3/4/09.

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Claims 1-3 remain rejected under 35 U.S.C. 102(e) as anticipated by Soltero et al. (US 6770625 B2), wherein the fact of intense pain in bone disorder Paget's disease is evidenced by the Yamamoto et al. (US 5059587) teaching at col. 1, lines 64-65.

In patent claim 62, Soltero et al. teach a method of treating a bone disorder such as "Paget's disease" (see col. 39, lines 56). Because intense pain is associated with "Paget's disease", treating said disease would necessarily lead to treatment of the pain. The method comprises orally administering to a subject in need a pharmaceutical composition comprising "calcitonin (CT)-drug-oligomer conjugate"; wherein CT is salmon calcitonin and wherein the conjugate is in a mono-dispersed mixture (patent claims 62, 76-79 and 81). Said "oligomer" preferably is "polyethylene glycol" (PEG) (see patent claim 80, and col. 24, lines 27, 35 and 36) linked to Lys¹¹ and Lys¹⁸ residues of calcitonin (patent claim 79). This inherently teaches instant method of claim 1.

Soltero et al. teach the structure: "Salmon calcitonin-[CO-(CH₂)₇-(OC₂H₄O)₇CH₃]₂" (see col. 31, lines 3-8) wherein "-(OC₂H₄O)₇" is PEG moiety subunits (see col. 25, lines 7-16), "CO-(CH₂)₇-" is a lipophilic moiety that preferably is a fatty acid moiety (see col. 25, lines 37-40), and wherein "2" in outside parentheses "[]" indicates two residues of CT peptide, i.e., Lys¹¹ and Lys¹⁸, are conjugated to the PEG moieties. This teaches the structural limitation of the "conjugate" of claim 3.

Soltero et al. teach that a (one) hydrolyzable bond between drug peptide and the "oligomer" (see col. 33, lines 47-50). In accordance with the claim 38 disclosure that PEG is coupled to the "oligomer" (i.e., calcitonin) via Lys¹¹ and Lys¹⁸ residues of calcitonin, thus, one of these two ε-lysine amino groups is conjugated to the PEG through said "hydrolyzable bond"

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while the other remains non-hydrolysable. This meets the structure of claim 2 “conjugate”.

Therefore, Soltero et al. inherently teach instant method of claim 2.

The applicants' response to the 102(e) rejection

At page 6, 6th paragraph, the response filed 7/6/09 submits that the priority of instant application dated back to 6/4/01 would obviate the 102 rejection. This is unpersuasive because instant claims 1-3 are entitled to have benefit of the earlier-filed provisional application 60482130 filed 6/24/03 but not entitled to the priority date 6/4/01 (see the reason set forth in the section "Priority" above). Thus, the 102 rejection is maintained.

New-Claim Rejections - 35 USC §103(a)

The text of Title 35, U.S. C 103(a) not included herein can be found in the prior Office action mailed 3/4/09.

[1] Claim 1 is rejected under 35 U.S.C. 35 U.S.C. 103(a) as unpatentable over as obvious over Lee et al. (US 6506730 B1).

In patent claims 1 and 2, Lee et al. teach a method of treatment comprising administering to mammal in need a pharmaceutical composition comprising polyethylene glycol (PEG) conjugated (PEGylated) calcitonin peptide. The PEGylation occurs at Lys¹¹ and Lys¹⁸ of calcitonin (see also Example 4); and wherein Paget's disease is treated; this disease has feature of pain from the bone absorption and calcitonin is obtained from Salmon (see col. 6, line 24-28).

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Lee et al. teach uniformed PEG-peptide conjugate wherein “uniformed” conjugate is equivalent to instant “mono-dispersed mixture conjugate”. These are applied to instant claim 1.

Lee et al. do not expressly teach use oral administering route.

It would have been obvious to one skilled in the art at the time the invention was made to determine the administration route, or/and parameters for suitable/optimal administration. Injection administration gives patients pain and has accompanying dangers; and thus, there remains a need to develop other routes for peptide administration (col. 1, lines 43-48, Lee et al.). Said development or determination is well within the purview of one skilled in the art, and therefore, said oral administration is considered to be prima facie obvious in the absence of any unexpected result.

[2] Claim 1 is rejected under 35 U.S.C. 103(a) as unpatentable over as obvious over Russo A. F. (US Pat. No. 5976788) in view of Komarova et al. (*Calcif. Tissue Int.* (2003, online published on 6/6/03) 73, 265-273) and Lee et al. (US Pat. No. 6506730 B1).

Russo teaches that calcitonin (CT) has therapeutic application for relieve pain such as “hypercalcemia pain” (see col. 9, lines 18-21).

Yet, Russo does not expressly teach use PEGylated CT for treating pain, wherein PEGylation includes PEGylation at Lys¹¹ and Lys¹⁸ residues of CT (claim1), nor expressly teach oral administering route.

Komarova et al. teach PEGylation of CT at Lys¹¹ and Lys¹⁸ residues and teach advantages of the PEGylation of enhance stability, increases half-life and decrease immunogenicity of said CT peptide (see p.265, right col., 2nd paragraph, and Fig. 1), as applicable to claim 1.

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Lee et al. teach that injection administration gives patients pain and has accompanying dangers; and thus, there is a need to develop other routes for peptide administration (col. 1, lines 43-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the PEGylated CT for treating the pain condition, wherein the PEG moiety is conjugated to the CT peptide directly through amino acids Lys¹¹ and Lys¹⁸. This is because Russo has taught usefulness of CT peptide for treating pain, and because Komarova et al. have taught that the CT peptide is PEGylated at of Lys¹¹ and Lys¹⁸ side chains. This Pegylation has advantage over the unpegylated peptide thereof in enhanced stability, increases half-life and decreased immunogenicity. Thus, it would have been obvious for one of ordinary skill in the art to substitute the PEGylated CT for the unPEGylated thereof with reasonable expectation of success.

In addition, considering that seeking for other administering route other than painful injection administration as taught by Lee et al., and further, considering that Russo's invention is directed to reducing pain, one of ordinary skill in the art (physician) would have chosen unpainful route such as oral administration which is well within the purview of one skilled in the art, and therefore, said oral route administration is considered to be *prima facie* obvious in the absence of any unexpected result. Therefore, combination of the references' teachings renders claim 1 *prima facie* obvious.

Examiner remark:

It is of note that instant “mono-dispersed conjugated” is considered to be an inherent property of the PEG-CT conjugate, because both instant conjugate and Komarova/Lee’s conjugate have identical covalent conjugation at Lys¹¹ and Lys¹⁸ side chains. This structural feature would determine biophysical property thereof such as mono-dispersion of the conjugate in solution. Structural feature is inherent property of a biomolecule, and products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

[3] Claim 2 is rejected under 35 U.S.C. 103(a) as unpatentable over as obvious over Russo A. F. (US Pat. NO. 5976788) in view of Komarova et al. (*Calcif. Tissue Int.* (2003, online published on 6/6/03) 73, 265-273), Katre et al. (US Pat. No. 491788) and Lee et al. (US Pat. No. 6506730 B1).

Russo teaches that calcitonin (CT) has therapeutic application for relieve pain such as “hypercalcemia pain” (see col. 9, lines 18-21).

Komarova et al. teach PEGylation of CT peptide and the advantages of the PEGylation: enhance stability, increases half-life and decrease immunogenicity of said CT peptide, wherein PEGylation occurs at Lys¹¹ and Lys¹⁸ side chains of the CT peptide (see p.265, right col., 2nd paragraph, and Fig. 1).

Yet, Russo and Komarova et al. do not expressly teach attachment of a non-hydrolysable linker between the peptide PEGylated and polyethylene glycol (PEG) nor expressly teach oral administration.

Katre et al. teach the hydrolysable bond between amine group of lysine and PEG moiety in the PEGylated peptide IL-2 (see col. 14, lines 28-36) wherein the amine group is lysine side chain (col. 8, lines 41-44).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to introduce a hydrolysable linker or bond between the peptide and PEG moiety. This is because Russo has taught usefulness of CT peptide for treating pain, and Komarova et al. have taught that the PEGylated CT peptide is advantageous over the unpegylated peptide at least in three aspects: enhanced stability, increases half-life and, and decreased immunogenicity. The hydrolysable bond between the PEG moiety and lysine amino side chain offers an advantage, i.e., it is particularly useful for recovering the peptide from the chromatographic column wherein the pH value of said column is close each other to that render the bond susceptible to hydrolysis (see col. 14, lines 28-36). Thus, one of ordinary skill in the art would have extended the Katre's results into production of the PEGylated CT peptides. The produced PEG-CT conjugates would expect to have benefit that the PEG polymer can be removed under alkaline condition and thus the CT peptide can be recovered from the hydrolysis.

In addition, considering that seeking for other administering route other than painful injection administration as taught by Lee et al., and further, considering that Russo's invention is directed to reducing pain, one of ordinary skill in the art (physician) would have chosen unpainful route such as oral administration which is well within the purview of one skilled in the art, and therefore, said oral route administration is considered to be *prima facie* obvious in the absence of any unexpected result. Therefore, combination of the references' teachings renders claim 1 *prima facie* obvious.

[4] Claim 3 is rejected under 35 U.S.C. 103(a) as unpatentable over as obvious over Russo A. F. (US Pat. NO. 5976788) in view of Komarova et al. (*Calcif. Tissue Int.* (2003, online published on 6/6/03)73,265-273), Katre et al. (US Pat. No. 491788), Crofts et al. (US 2003/0017203 A1) and Lee et al. (US Pat. No. 6506730 B1).

Russo teaches that CT therapeutic use in relieving pain, e.g., "hypercalcemia pain" (col. 9, lines 18-21).

Komarova et al. teach PEGylation of CT peptide and the advantages of the PEGylation: enhance stability, increase half-life and decrease immunogenicity of said CT peptide (p.265, right col., 2nd paragraph) wherein the conjugated PEG polymer has 7 PEG subunits (see Fig.1).

Yet, Russo and Komarova et al. do not expressly teach attachment of a carboxylic acid as a linker between the peptide and PEG, nor expressly teach oral administration.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a fatty acid (a type of "carboxylic acid") into PEG conjugated the CT peptide between the conjugation sites: Lys¹¹ or Lys¹⁸ of said peptide and the PEG moieties. This is because Russo has taught usefulness of CT peptide for treating pain, and Komarova et al. have taught that the PEGylated CT peptide is advantageous over the unpegylated peptide in at least three aspects: enhanced stability, increases half-life and, and decreased immunogenicity. It has been known that a biological difficulty for salmon CT to penetrate the mucus membranes which limits bioavailability of the calcitonin (see [0004], lines 11-15, Crofts et al.). Upon reading the Crofts reference, one skilled in the art would have realized the problem of bioavailability of the calcitonin peptide caused by the **membrane penetration**, and would have known that the

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incorporation of fatty acid which is known membrane anchor molecule. Thus, one of ordinary skill in the art would have modified the PEGylated CT peptide further to incorporate fatty acid (a carboxylic acid) into said peptide in order to improve the membrane penetration ability of the PEGylated CT.

In addition, considering that seeking for other administering route other than painful injection administration as taught by Lee et al., and further, considering that Russo's invention is directed to reducing pain, one of ordinary skill in the art (physician) would have chosen unpainful route such as oral administration which is well within the purview of one skilled in the art, and therefore, said oral route administration is considered to be *prima facie* obvious in the absence of any unexpected result. Therefore, combination of the references' teachings renders claim 1 *prima facie* obvious.

* *Examiner remark*: the inherent property of the "mono-dispersed" of the PEGylated CT conjugate has been discussed above., which is applied to the above 103(a) rejections [2] and [3].

The applicants' response to the 103 rejections

At pages 8-10, the response filed 7/6/09 submits that Russo does not teach the PEGylated CT for treating pain (p.9, paragraphs 2 and 5), and assert that the Komarova et al. is not competent prior art (p.10, 2nd paragraph). Thus, the response requests withdrawal of the rejections.

The applicants' arguments are found unpersuasive because Komarova et al. is published on 6/6/03 which antedates instant priority date 6/24/03 (see the above discussion under section "Priority"), and because combination of the Russo's and Komarova's teachings renders the

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claims obvious (see above discussion). Russo has taught therapeutic use of calcitonin (CT) in relieve pain; and, Komarova et al. have taught PEGylation renders the CT peptide more stable in vivo as well as less immunogenic. Thus, it would have been obvious to combine the teachings thereof and arrived at the claimed method. Therefore, the 103 rejections stand.

Maintained-Claim Rejection -Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[1] Claims 1-2 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 11 and 12 of US Pat. No. 7084121 (**121**). Although the conflicting claims are not identical, they are not patentable distinct from each other because of the following reasons.

Claims 11-12 of 121’ disclose a method of treating osteoporosis Paget’s disease (a bone disorder associated with intense pain in some stage thereof, see col. 1, lines 47-59) comprising

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administering PEGylated calcitonin wherein the calcitonin peptide is coupled to at least one PEG moiety encompassing "two PEG moieties". Since the calcitonin peptide contains two internal lysine residues Lys¹¹ or Lys¹⁸, claims 12-13 are obvious variation of instant claim 1.

Claim 6 of 121' discloses that calcitonin is covalently coupled to the polyethylene glycol moiety by a hydrolyzable bond, a non-hydrolyzable bond or both; and thus, claims 11-12 together with claim 6 are obvious variation of instant claim 2.

Claims 1-3 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38, 62 and 76-80 of US Pat. No. 6770625 (625). Although the conflicting claims are not identical, they are not patentable distinct from each other because of the following reasons.

Claims 38, 62 and 76-80 of 625' disclose a method of treating a done disorder such as "Paget's disease" (col. 39, lines 56, the specification) which has intense pain symptom comprising administering to a subject in need a pharmaceutical composition comprising "calcitonin (CT)-drug-oligomer conjugate"; wherein CT is salmon calcitonin (patent claims 38 and 78), and wherein the "oligomer" preferably is "polyethylene glycol" (PEG) (see col. 24, lines 27, 35 and 36, and patent claim 80) linked to Lys¹¹ and Lys¹⁸ residues of calcitonin (patent claims 38 and 79). This is an obvious variation of instant claim 1.

Claim 80 of 625' disclose that "CT-drug-oligomer conjugate" inherently comprises a lipophilic moiety, e.g., a fatty acid moiety [(see also col. 3, lines 3-8, the structure of the oligomer: "Salmon calcitonin-[CO-(CH₂)₇-(OC₂H₄O)₇CH₃]₂" wherein "-(OC₂H₄O)₇" is PEG subunits (see col. 25, lines 7-16), "CO-(CH₂)₇-" is considered to be a lipophilic moiety that

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preferably is a fatty acid moiety (see col. 25, lines 37-40), and wherein “2” in outside parentheses indicates two lysine residues Lys¹¹ and Lys¹⁸ of the CT peptide conjugated to PEG]. The disclosure teaches a linker which is a carboxylic acid such as glycocholate (col. 22, lines 52-57,). These together are obvious variation of instant claim 3.

Each drug peptide (CT) is conjugated to “oligomer” (PEG polymers) through a hydrolysable bone (col. 33, lines 47-50, the specification). Claims 38 and 79 disclose that PEG is linked to the CT peptide via Lys¹¹ and Lys¹⁸ of the CT peptide; this suggests that thus, one of these two ϵ -lysine amino groups are conjugated to the PEG through said “hydrolysable bone” while the other remains non-hydrolysable. Therefore, claim 62 is an obvious variation of instant claim 2.

The applicants' response to the ODP rejections

At pages 10-12, the response filed 7/6/09 submits that because of the submission of the terminal disclaimer (TD) for 7084121, the ODP rejection of claims 1 and 2 over 7084121 should be withdrawn (page 10, 4th paragraph). This is unpersuasive because said TD is disapproved by the Office. Applicants may resubmit TD in this regard.

Also, the response submits that the claims of 625' patent differ from instant claims (p.10, last paragraph), and that the Office has not provided factual basis and/or rationale to support conclusion of claims 1-3 are obvious variation of the claims of 625' (p.12, paragraphs 1 and 2). Thus, the response requests withdrawal of the ODP rejections of claims 1-3 over 625'. The applicants' arguments are found unpersuasive because the obviousness of instant claims 1-3 over the claims of 625' has been discussed in detail (see above), and because factual indicia of

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the ODP set forth above come from instant claims and disclosure not from otherwise reference.

Thus, the ODP rejection is deemed to be proper and thus stands.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Liu whose telephone number is (571)272-0949. The examiner can normally be reached on Monday-Friday, 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656

/ANAND U DESAI/

Primary Examiner, Art Unit 1656

September 30, 2009